Remarks

Claims 1 to 13 were in the application as filed. Claims 14 to 22 were added in the Preliminary Amendment filed on December 22, 1999. Claim 8 was canceled by the Amendment filed on October 23, 2003.

Claim 1 has been amended as follows: the solid composition for oral administration is limited to tablet forms (support for this amendment can be found in the specification, for example, on page 3, line 37 and in the examples); the nonionic hydrophilic surfactant is selected from poloxamers (support for this amendment can be found in the specification, for example, on page 4, line 7 and in the examples); the proportion of nonionic hydrophilic surfactant, expressed by weight of the active principle in base form, is changed from 1% to 50% to 5 to 15% (support for this amendment can be found in the specification, for example, on page 4, lines 36-37 and in the examples); and polysorbate surfactants are specifically excluded from the compositions (see e.g. *In re Johnson*, 558 F.2d 1008, 194 U.S.P.Q. 187 (CCPA 1997)).

Claims 6, 12, and 13 have been amended to essentially incorporate the above-described amendments to Claim 1 therein. Claim 18 has been amended and Claims 5, 9, 10 and 17 have been canceled to remove redundant subject matter.

No new matter had been added by these amendments.

As presently amended, Claims 1 to 4, 6 to 7, 11 to 16, and 18 to 22 are pending in this application.

Applicants filed an Amendment and Remarks on February 15, 2006, in response to the Final Office Action mailed November 16, 2005. An Advisory Action was mailed on March 31, 2006, wherein the Examiner stated that Applicants' amendments submitted on February 15, 2006 were not entered.

Applicants filed a Notice of Appeal in the instant case on April 14, 2006. However, the Request for Continued Examination submitted herewith is being filed in lieu of a Brief on Appeal.

Obviousness Rejections

In the Final Office Action dated November 16, 2005, the Examiner maintained the rejection of Claims 1 to 7 and 9 to 22 under 35 U.S.C. § 103(a) as being, the Examiner alleged, unpatentable over the Physician's Desk Reference ("PDR") in view of US Patent No. 4,944,949, issued to Story et al. ("Story") and Martin-Algarra et al., International Journal of Pharmaceutics, 122 (1995), pp. 1-8 ("Martin-Algarra"). In the Advisory Action dated March 31, 2006, the Examiner indicated that "[a]lthough applicant has added the words 'selected from poloxamers' to claim 1, the claim language comprising leaves the claim open for the inclusion of unspecified ingredients, even in major amounts. Thus, it does not exclude the polysorbate of Martin Algarra et al." (page 2).

This rejection is traversed and reconsideration and withdrawal thereof are respectfully requested for the reasons given hereinbelow.

The instant invention provides solid pharmaceutical compositions in tablet form containing a benzofuran derivative with antiarrhythmic activity as active principle, such as amiodarone and dronedarone. The formulation of such a benzofuran derivative was a challenge given its low solubility in aqueous medium, particularly in the intestine medium (neutral medium), and given its variability of absorption depending on the intake of food (see Specification at page 1, line 36 to page 3, line 12).

The primary reference cited by the Examiner, the PDR, merely teaches the low solubility of amiodarone.

The secondary Story reference teaches the addition of surfactants to a formulation which is in liquid form for other types of poorly soluble active principles, namely non-steroidal anti-inflammatory drugs (NSAIDs) (see column 4, lines 39-58 and the examples, which all relate to solutions or to liquid-filled capsules). Story therefore provides no guidance to one skilled in the art searching for a solid pharmaceutical composition in tablet form.

In addition, Story's formulations contain a far greater ratio of surfactant to active principle compared to Applicants' claimed formulations (see column 12, lines 56-61: the

surfactant is used at a 5.7 to 50 fold greater amount than the active principle). While acknowledging that Applicants' modifications result in "great improvement and utility over prior art," the Examiner indicates that "where general conditions of claim are disclosed in the prior art, it is not inventive to discover optimum or workable ranges by routine experimentation" and that "the determination of optimal values within a disclosed range is generally considered obvious" (Advisory Action, page 2). However, as previously indicated, the amount of surfactant required in Applicants' compositions is *not* within the disclosed range, but is present in a significantly lesser ratio compared with the active principle than the amount taught by Story.

Furthermore, even though Story mentions poloxamers among numerous surfactants available in pharmaceutical science (enumerated through columns 5 to 7), *none* of the specific formulations exemplified by Story (examples 1 to 127, columns 12 to 22) use poloxamer surfactants, thereby deterring one skilled in the art from using such surfactants. Accordingly, Story provides no motivation to choose a poloxamer surfactant, as recited in presently amended claim 1.

Therefore, even if one of skill in the art combined the PDR and the Story teachings, they would not arrive at the invention as recited in presently amended claim 1, wherein the composition is in the form of a tablet *and* wherein the quantity of surfactant is 5-15% by weight of the active principle *and* wherein the surfactant chosen is a poloxamer.

The third reference cited by the Examiner, Martin-Algarra, describes the effects of polysorbate 80 on the absorption of amiodarone. As with Story, this reference similarly fails to teach or suggest a composition in tablet form. In addition, Martin-Algarra fails to teach the use of poloxamers as required by presently amended claim 1 of the instant invention.

In the Advisory Action, the Examiner indicated that the word "comprising" does not leave out additional unspecified ingredients. However, to establish a prima facie case of obvious the question is whether Martin-Algarra teaches or suggests the use of poloxamers in Applicants claimed compositions, not whether Applicants claims can technically include such surfactants. While disagreeing with the Examiner's contention that it would be obvious to include polysorbates because the claim language comprising leaves the claim open for unspecified ingredients, Applicants have amended claim 1 so as to specifically exclude polysorbates.

It is therefore apparent that, first, there is no suggestion or motivation to modify the three prior art references analyzed above or to combine them; second, there could not be a reasonable expectation of success since neither Story nor Martin-Algarra teaches or suggests a solid pharmaceutical composition in tablet form; and finally, the prior art references neither teach nor suggest all of the features now recited in presently amended claim 1.

The solid pharmaceutical compositions in tablet form for oral administration as recited in presently amended claim 1 are, therefore, non-obvious over the prior art references.

In the Final Office Action dated November 16, 2005, the Examiner also maintained the rejection of Claims 2, 7, 11, 12, 16 and 18 to 22 under 35 U.S.C. § 103(a) as being, the Examiner alleged, unpatentable over Martin-Algarra.

This rejection is traversed and reconsideration and withdrawal thereof are respectfully requested for the reasons given hereinbelow.

As stated above, Martin-Algarra fails to teach or suggest a pharmaceutical composition in tablet form for oral administration of a benzofuran derivative, or the use of a poloxamer surfactant in such a composition. Additionally, Martin-Algarra fails to provide the requisite "reasonable expectation of success" for preparing a pharmaceutical composition in tablet form for oral administration of a benzofuran derivative. Accordingly, the rejection of Claims 2, 7, 11, 12, 16 and 18 to 22 should be withdrawn.

Double Patenting Rejection

In the Final Office Action dated November 16, 2005, the Examiner maintained the rejection of Claims 1 to 7 and 9 to 22 under the judicially created doctrine of obviousness-type double patenting as being, the Examiner alleged, unpatentable over claims 1 to 30 of US Patent No. 6,143,778. The Examiner acknowledged that there is nothing in US 6,143,778 to suggest lyophilizing the composition in the patent, but the Examiner nevertheless concluded that "to incorporate said liquid composition into a capsule capable of containing liquid for oral administration would have been obvious." (Final Office Action page 4).

In view of the above-described amendments to Claim 1, limiting the invention to compositions in the form of tablets, this objection is believed overcome and withdrawal thereof is respectfully requested.

There being no remaining issues, this application is believed in condition for favorable reconsideration and early allowance, and such actions are earnestly solicited.

The Commissioner is hereby authorized to charge any additional fees which may be required by this paper, or credit any overpayment to Deposit Account No. 18-1982.

Respectfully submitted,

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Dated

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